

AMENDMENTS

IN THE CLAIMS

Claims 1-66, 68, 70, 72, 74, 75, 78, 80, 85, 93, 100-112, 115, 121-126, 129, 151, 153, and 154 are canceled.

Claims 67, 69, 71, 73, 76, 77, 79, 81-84, 86-92, 94-99, 113, 114, 116-120, 137-150, 152, and 155 are pending in this Application.

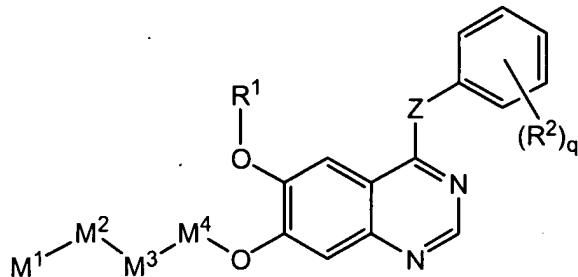
Claims 127, 128, and 130-136 were provisionally withdrawn and are subject to rejoinder.

Claims 67, 113, 114, 116, 127, 137-143, 146, 149, 150, 152, and 155 are currently amended.

Claims 69, 71, 73, 76, 77, 79, 81-84, 86-92, 94-99, 117-120, 128-136, 144, 145, 147, and 148 were previously presented.

Claims 1-66. (canceled)

67. (currently amended) A compound of Formula I,



I

or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof, wherein,

R<sup>1</sup> is methyl;

R<sup>2</sup> is selected from halogen, trihalomethyl, -CN, -NH<sub>2</sub>, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>4</sup>, -S(O)<sub>0-2</sub>R<sup>4</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>4</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(=O)N(R<sup>3</sup>)R<sup>4</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>4</sup>, -N(R<sup>3</sup>)C(=O)R<sup>3</sup>, -N(R<sup>3</sup>)CO<sub>2</sub>R<sup>4</sup>, -C(=O)R<sup>3</sup>, lower alkyl, lower alkenyl, and lower alkynyl;

R<sup>3</sup> is -H or R<sup>4</sup>;

$R^4$  is selected from lower alkyl; lower alkyl substituted with one, two, or three halogen; aryl; aryl substituted with one, two, or three halogen; and unsubstituted lower arylalkyl; heterocyclyl; and lower heterocyclylalkyl; or

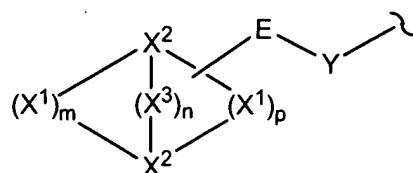
$R^3$  and  $R^4$ , when taken together with a common nitrogen to which they are attached, form a five to seven membered heterocyclyl optionally containing at least one additional heteroatom selected from N, O, S, and P where the five to seven membered heterocyclyl is morpholinyl, pyrrolidinyl, piperidinyl, or piperazinyl optionally substituted by one, two, or three alkyl;

$q$  is 0, 1, 2, 3, 4, or 5;

$Z$  is  $-NR^5-$ ;

$R^5$  is  $-H$ ;

$M^1-M^2-M^3-M^4$ - together are according to formula II:



II

wherein  $X^1$ ,  $X^2$ , and optionally  $X^3$ , represent the atoms of a saturated bridged ring system, said saturated bridged ring system containing up to three annular

heteroatoms represented by any of  $X^1$ ,  $X^2$ , and  $X^3$ ; wherein,

each  $X^1$  is independently selected from  $-C(R^6)R^7-$ ,  $-O-$ ,  $-S(O)_{0-2}-$ , and  $-NR^8-$ ;

each  $X^2$  is independently a bridgehead methine optionally substituted with  $R^6$ , or a bridgehead nitrogen;

each  $X^3$  is independently selected from  $-C(R^6)R^7-$ ,  $-O-$ ,  $-S(O)_{0-2}-$ , and  $-NR^8-$ ;

provided, for  $X^1$ ,  $X^2$ , and  $X^3$ , there are no nitrogen-nitrogen annular bonds nor geminal di-nitrogen substitutions;

$E$  is absent;

$Y$  is  $-CH_2-$  provided that  $Y$  is not directly attached to any heteroatom represented by  $X^1$ ,  $X^2$  or  $X^3$ ; or

$m$  and  $p$  are each independently 1, 2, 3, or 4;

n is 0, 1, or 2, when n is zero, then there is a direct single bond between the two bridgehead  $X^2$ 's;

$R^6$  and  $R^7$  are each independently selected from -H, halogen, trihalomethyl, -CN, -NH<sub>2</sub>, -NO<sub>2</sub>, -OR<sup>3</sup>, -N(R<sup>3</sup>)R<sup>4</sup>, -S(O)<sub>0-2</sub>R<sup>4</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>4</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>4</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>4</sup>, -N(R<sup>3</sup>)C(O)R<sup>3</sup>, -NCO<sub>2</sub>R<sup>3</sup>, -C(O)R<sup>3</sup>, lower alkyl, aryl, and unsubstituted lower arylalkyl, ~~heterocyclyl~~ optionally substituted with one alkyl, and lower ~~heterocyclylalkyl~~; or

$R^6$  and  $R^7$ , when taken together are oxo; or

$R^6$  and  $R^7$ , when taken together with a common carbon to which they are attached, form a three- to seven-membered spirocyclyl optionally containing at least one additional heteroatom selected from N, O, S, and P and wherein the spirocyclic ring is optionally substituted with one or two alkyl; and

$R^8$  is selected from R<sup>3</sup>, -SO<sub>2</sub>N(R<sup>3</sup>)R<sup>4</sup>, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>4</sup>, -SO<sub>2</sub>R<sup>4</sup>, and -C(O)R<sup>3</sup>;

with the proviso that when Y is a C<sub>1-3</sub> alkylene linker, E is absent, Z is -NH- or -N(CH<sub>3</sub>)-, R<sup>1</sup> is a C<sub>1-3</sub> alkyl, R<sup>2</sup> is -H or halogen, n = 0, and the atoms X<sup>1</sup> of one bridge of the saturated bridged ring system, when combined with both bridgehead atoms, X<sup>2</sup>, of the saturated bridged ring system, represent:

either a pyrrolidine ring or a piperidine ring, and any atom, X<sup>1</sup> or X<sup>2</sup>, of either of said pyrrolidine ring or said piperidine ring is attached to Y; then the other bridge of said saturated bridged ring system cannot be any one of -OC(O)CH<sub>2</sub>-, -CH<sub>2</sub>OC(O)-, -OC(O)CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>OC(O)CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>OC(O)-, -OC(O)CH<sub>2</sub>NH-, -OC(O)CH<sub>2</sub>N(C<sub>1-4</sub>alkyl)-, and -OC(O)CH<sub>2</sub>O-; and

either a piperazine ring or a 4-(C<sub>1-4</sub> alkyl)-piperazine ring, and any atom, X<sup>1</sup> or X<sup>2</sup>, of either of said piperazine ring or said 4-(C<sub>1-4</sub> alkyl)-piperazine ring is attached to Y; then the other bridge of said saturated bridged ring system, only when attached via the 2- and the 3-position of either of said piperazine ring or said 4-(C<sub>1-4</sub> alkyl)-piperazine ring, cannot be one

of  $-\text{CH}_2\text{OC(O)CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{OC(O)}$ -, and either of the two aforementioned bridges substituted by one or two  $\text{C}_{1-2}$ alkyl groups; and a piperazine ring, and any atom,  $\text{X}^1$  or  $\text{X}^2$ , of said piperazine ring is attached to Y; then the other bridge of said saturated bridged ring system, only when attached via the 3- and the 4-position of said piperazine ring, cannot be  $-\text{C(O)OCH}_2\text{CH}_2-$ ,  $-\text{CH}_2\text{OC(O)CH}_2-$ ,  $-\text{C(O)OCH}_2\text{CH}_2-$  substituted with one or two  $\text{C}_{1-2}$ alkyl groups, or  $-\text{CH}_2\text{OC(O)CH}_2-$  substituted with one or two  $\text{C}_{1-2}$ alkyl groups (but only when the four above mentioned bridges are attached to the 3-position of said piperazine ring via their left-hand end as depicted above); and

a 2-oxomorpholine ring, said 2-oxomorpholine ring attached to Y via its 4-position; then the other bridge of said saturated bridged ring system, only when attached via the 5- and the 6-position of said 2-oxomorpholine ring, cannot be one of  $-(\text{CH}_2)_g-$ ,  $-\text{CH}_2\text{WCH}_2-$ ,  $-\text{CH}_2\text{WCH}_2\text{CH}_2-$ , and  $-\text{CH}_2\text{CH}_2\text{WCH}_2-$ , wherein W is  $-\text{O}-$ ,  $-\text{S(O)}_{0-2}-$ ,  $-\text{NH}-$ , or  $-\text{N}(\text{C}_{1-4}\text{ alkyl})-$  and wherein g is 2, 3, or 4.

68. (canceled)

69. (previously presented) The compound according to claim 67, wherein  $\text{R}^2$  is selected from halogen, trihalomethyl,  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{OR}^3$ , and lower alkyl; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

70. (canceled)

71. (previously presented) The compound according to claim 69, wherein the saturated bridged ring system has a geometry selected from the group consisting of [4.4.0], [4.3.0], [4.2.0], [4.1.0], [3.3.0], [3.2.0], [3.1.0], [3.3.3], [3.3.2], [3.3.1], [3.2.2], [3.2.1], [2.2.2], and [2.2.1]; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

72. (canceled)

73. (previously presented) The compound according to claim 71, wherein q is 1, 2, or 3; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

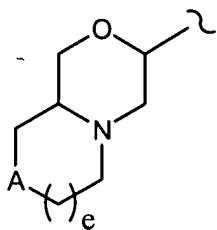
Claims 74-75 (canceled)

76. (previously presented) The compound according to claim 73, wherein the saturated bridged ring system has a geometry selected from the group consisting of [4.4.0], [4.3.0], [4.2.0], [4.1.0], [3.3.0], [3.2.0], and [3.1.0]; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

77. (previously presented) The compound according to claim 76, wherein said saturated bridged ring system contains one or two annular nitrogens, said one or two annular nitrogens are selected from  $-NR^8-$ , when  $X^1$ , and a bridgehead nitrogen, when  $X^2$ ; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

78. (canceled)

79. (previously presented) The compound according to claim 77 wherein said saturated bridged ring system is according to formula III;



III

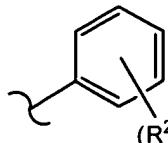
wherein A is selected from  $-O-$ ,  $-S(O)_{0-2}-$ ,  $-NR^8-$ , and absent; and e is 0 or 1; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

80. (canceled)

81. (previously presented) The compound according to claim 79 wherein A is selected from  $-NR^8-$ , wherein  $R^8$  is selected from -H, lower alkyl,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^4$ ,  $-SO_2R^4$ , and  $-C(O)R^3$ ;  $-O-$ ; and absent; or a single stereoisomer, racemate,

enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

**82. (previously presented)** The compound according to claim 81, wherein



$(R^{2q})_q$  of I is selected from:

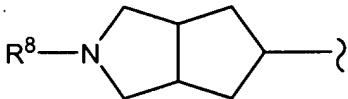
and

and

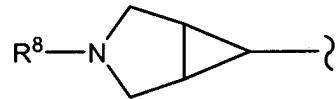
wherein  $R^{2a}$ ,  $R^{2b}$ , and  $R^{2c}$  are each independently selected from F, Cl, and Br; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

**83. (previously presented)** The compound according to claim 82, wherein  $R^{2a}$  is F,  $R^{2b}$  is Cl, and  $R^{2c}$  is either Cl or Br; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

**84. (previously presented)** The compound according to claim 77, wherein said saturated bridged ring system is according to either formula V or formula VI;



V

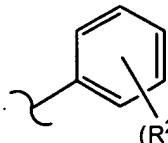


VI

wherein  $R^8$  is selected from -H, lower alkyl,  $-CO_2R^3$ ,  $-C(O)N(R^3)R^4$ ,  $-SO_2R^4$ , and  $-C(O)R^3$ ; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

**85. (canceled)**

**86. (previously presented)** The compound according to claim 84, wherein



$(R^{2q})_q$  of I is selected from:

and

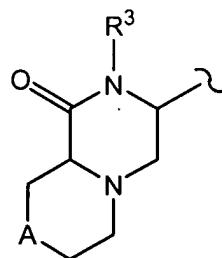
and

wherein  $R^{2a}$ ,  $R^{2b}$ , and  $R^{2c}$  are each independently selected from F, Cl, and Br; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

87. (previously presented) The compound according to claim 86, wherein R<sup>2a</sup> is F, R<sup>2b</sup> is Cl, and R<sup>2c</sup> is either Cl or Br; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

88. (previously presented) The compound according to claim 87, wherein R<sup>8</sup> is methyl or ethyl; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

89. (previously presented) The compound according to claim 77, wherein said saturated bridged ring system is according to formula VII;



VII

wherein A is selected from -O-, -S(O)<sub>0-2</sub>-, -NR<sup>8</sup>-, -CR<sup>6</sup>R<sup>7</sup>-, and absent; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

90. (previously presented) The compound according to claim 89, wherein R<sup>3</sup> is selected from -H and alkyl; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

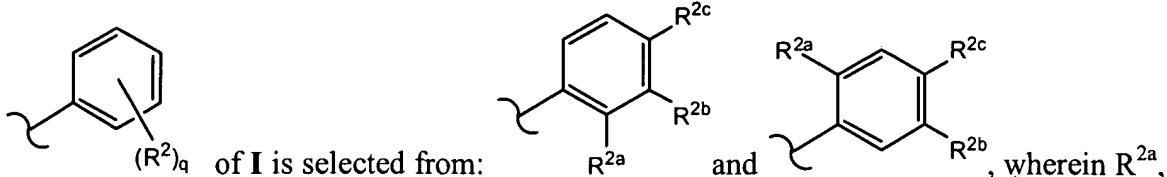
91. (previously presented) The compound according to claim 90 wherein A is either -C(R<sup>6</sup>)R<sup>7</sup> or absent; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

92. (previously presented) The compound according to claim 91, wherein A is either -CH<sub>2</sub>- or absent; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

93. (canceled)

94. (previously presented) The compound according to claim 92, wherein q is 3; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

95. (previously presented) The compound according to claim 94, wherein



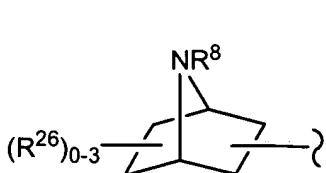
wherein R<sup>2a</sup>, R<sup>2b</sup>, and R<sup>2c</sup> are each independently selected from F, Cl, and Br; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

96. (previously presented) The compound according to claim 95, wherein R<sup>2a</sup> is F, R<sup>2b</sup> is Cl, and R<sup>2c</sup> is either Cl or Br; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

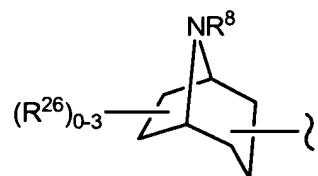
97. (previously presented) The compound according to claim 73, wherein the saturated bridged ring system has a geometry selected from the group consisting of [3.3.1], [3.2.1], and [2.2.1]; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

98. (previously presented) The compound according to claim 97, wherein said saturated bridged ring system contains one or two annular nitrogens, said one or two annular nitrogens are selected from -NR<sup>8</sup>-, when X<sup>1</sup>, and a bridgehead nitrogen, when X<sup>2</sup>; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

99. (previously presented) The compound according to claim 98, wherein said saturated bridged ring system is according to formula VIII or formula IX;



VIII

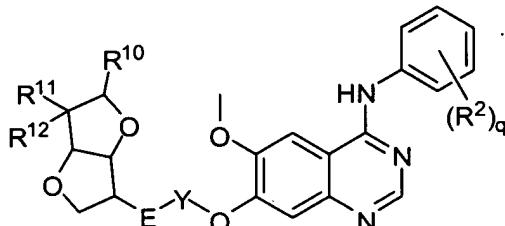


IX

wherein R<sup>8</sup> is selected from -H, lower alkyl, -CO<sub>2</sub>R<sup>3</sup>, -C(O)N(R<sup>3</sup>)R<sup>4</sup>, -SO<sub>2</sub>R<sup>4</sup>, and -C(O)R<sup>3</sup>; and R<sup>26</sup> is C<sub>1-3</sub> alkyl; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

Claims 100-112. (canceled)

113. (currently amended) A compound of Formula Ia,



Ia

or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof, wherein,

q is 1, 2, or 3;

R<sup>2</sup> is selected from halogen, trihalomethyl, -CN, -NO<sub>2</sub>, -OR<sup>3</sup>, lower alkyl, and piperazinyl substituted with methyl;

Y is -CH<sub>2</sub>-;

E is absent;

R<sup>3</sup> is -H or R<sup>4</sup>;

R<sup>4</sup> is selected from lower alkyl; lower alkyl substituted with one, two, or three halogen; aryl; aryl substituted with one, two, or three halogen; and unsubstituted lower arylalkyl; heterocyclyl; and lower heterocyclylalkyl; or

R<sup>3</sup> and R<sup>4</sup>, when taken together with a common nitrogen to which they are attached, form a five to seven membered heterocyclyl optionally containing at least one additional heteroatom selected from N, O, S, and P where the five to seven membered heterocyclyl is morpholinyl, pyrrolidinyl, piperidinyl, or piperazinyl optionally substituted by one, two, or three alkyl;

R<sup>10</sup> is selected from -H, alkyl, and -OR<sup>13</sup>; and R<sup>11</sup> and R<sup>12</sup> are each independently selected from -H, -CF<sub>3</sub>, -F, -N(R<sup>3</sup>)R<sup>4</sup>, -N(C=O)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>, -S(O)<sub>0-2</sub>R<sup>13</sup>, -OR<sup>13</sup>, -OS(O)<sub>2</sub>alkyl, and -NH<sub>2</sub>, and alkyl substituted with alkoxy; or

$R^{10}$  is selected from -H, and -OR<sup>13</sup>; and R<sup>11</sup> and R<sup>12</sup>, when taken together, are oxo, exo-alkenyl, or when taken together with the carbon to which they are attached, form a three- to seven-membered spirocyclyl; and

$R^{13}$  is selected from -H;  $-C(=O)R^4$ ; lower alkenyl; unsubstituted lower arylalkynyl; ~~lower heterocyclylalkynyl~~; lower alkenyl; unsubstituted lower arylalkenyl; lower alkyl; lower alkyl substituted with one, two, or three halogen; unsubstituted lower arylalkyl; and aryl; ~~lower heterocyclylalkyl~~ optionally substituted with one alkyl; and heterocyclyl; or

two  $R^{13}$ 's, when taken together, form 1) a corresponding spirocyclic ketal from R<sup>11</sup>, R<sup>12</sup> and the carbon to which they are attached, when R<sup>11</sup> and R<sup>12</sup> are both -OR<sup>13</sup>, or 2) a corresponding cyclic ketal from  $R^{10}$  and one of R<sup>11</sup> and R<sup>12</sup>, and the corresponding carbons to which they are attached, when R<sup>10</sup> is -OR<sup>13</sup>, and at least one of R<sup>11</sup> and R<sup>12</sup> is also -OR<sup>13</sup>, and which spirocyclic and cyclic ketal are independently ketal is optionally substituted with one or two alkyl.

114. (currently amended) The Compound of Claim 113 wherein

q is 1, 2, or 3;

$R^2$  is selected from halogen, trihalomethyl, -CN, -NO<sub>2</sub>, -OR<sup>3</sup>, and lower alkyl;

Y is -CH<sub>2</sub>-;

E is absent;

$R^3$  is -H or R<sup>4</sup>;

$R^4$  is selected from lower alkyl; lower alkyl substituted with one, two, or three halogen; aryl; aryl substituted with one, two, or three halogen; and unsubstituted lower arylalkyl; ~~heterocyclyl~~; and ~~lower heterocyclylalkyl~~; or

$R^3$  and  $R^4$ , when taken together with a common nitrogen to which they are attached, form ~~a five to seven membered heterocyclyl optionally containing at least one additional heteroatom selected from N, O, S, and P where the five to seven membered heterocyclyl is morpholinyl, pyrrolidinyl, piperidinyl, or piperazinyl~~ optionally substituted by one, two, or three alkyl;

$R^{10}$  is selected from -H, alkyl, and -OR<sup>13</sup>; and R<sup>11</sup> and R<sup>12</sup> are each independently selected from -H, -CF<sub>3</sub>, -F, -N(R<sup>3</sup>)R<sup>4</sup>, -N(C=O)R<sup>3</sup>, -N(R<sup>3</sup>)SO<sub>2</sub>R<sup>3</sup>,

$-S(O)_{0-2}R^{13}$ , and  $-OR^{13}$ ; or

$R^{10}$  is selected from -H, and  $-OR^{13}$ ; and  $R^{11}$  and  $R^{12}$ , when taken together, are oxo, exo-alkenyl, or when taken together with the carbon to which they are attached, form a three- to seven-membered spirocyclyl; and

$R^{13}$  is selected from -H;  $-C(=O)R^4$ ; lower alkynyl; unsubstituted lower arylalkynyl; ~~lower heterocyclylalkynyl~~; lower alkenyl; unsubstituted lower arylalkenyl; lower alkyl; lower alkyl substituted with one, two, or three halogen; unsubstituted lower arylalkyl; and aryl; ~~lower heterocyclylalkyl~~ optionally substituted with one alkyl; and heterocyclyl; or

two  $R^{13}$ 's, when taken together, form 1) a corresponding spirocyclic ketal from  $R^{11}$ ,  $R^{12}$  and the carbon to which they are attached, when  $R^{11}$  and  $R^{12}$  are both  $-OR^{13}$ , or 2) a ~~corresponding cyclic ketal from  $R^{10}$  and one of  $R^{11}$  and  $R^{12}$ , and the corresponding carbons to which they are attached, when  $R^{10}$  is  $OR^{13}$ , and at least one of  $R^{11}$  and  $R^{12}$  is also  $OR^{13}$~~ ; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

115. (canceled)

116. (currently amended) The compound according to claim 114, wherein one of  $R^{11}$  and  $R^{12}$  is  $-OR^{13}$ , wherein  $R^{13}$  is selected from -H,  $-C(=O)R^4$ , lower alkyl, and lower alkyl substituted with one, two, or three halogen; and  $R^{10}$  and the other of  $R^{11}$  and  $R^{12}$  are both -H; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

117. (previously presented) The compound according to claim 114, wherein one of  $R^{11}$  and  $R^{12}$  is -F; and  $R^{10}$  and the other of  $R^{11}$  and  $R^{12}$  are both -H; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

118. (previously presented) The compound according to claim 114, wherein  $R^{13}$  is a lower alkyl group containing at least one fluorine substitution thereon; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

119. **(previously presented)** The compound according to claim 114, wherein q is 2 or 3; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

120. **(previously presented)** The compound according to claim 119, wherein each R<sup>2</sup> is independently selected from -F, -Cl, -Br, -CF<sub>3</sub>, -CH<sub>3</sub>, and -OR<sup>25</sup>; wherein R<sup>25</sup> is either methyl or aryl, each optionally substituted with one to three halogens; or a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

Claims 121-126 **(canceled)**

127. **(provisionally-withdrawn, currently-amended, subject to rejoinder)** A method of treating a disease or a disorder associated with abnormal cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of the compound of Claim 67, 147, or 148 ~~Formula I or Ia~~ optionally together with a pharmaceutically acceptable carrier.

128. **(provisionally-withdrawn, subject to rejoinder)** The method of Claim 127 where the disease is cancer.

129. **(provisionally-withdrawn, canceled)**

130. **(provisionally-withdrawn, subject to rejoinder)** The method of Claim 127 where the cancer is selected from non-small cell lung cancer, glioblastoma, pancreatic cancer, cancer of the nervous system, cancer of the large bowel, multiple myeloma, undifferentiated small cell bronchogenic carcinoma, gastrointestinal cancer, esophageal cancer, malignant melanoma, neuroblastoma, osteosarcoma, ovarian cancer, endometrial cancer, cervical cancer, bladder cancer, urethral cancer, and prostate cancer.

131. **(provisionally-withdrawn, subject to rejoinder)** The method of Claim 127 where the cancer is selected from non-small cell lung cancer, glioblastoma, pancreatic cancer, cancer of the nervous system, cancer of the large bowel, neuroblastoma, and gastrointestinal cancer.

132. **(provisionally-withdrawn, subject to rejoinder)** The method of Claim 127 where the cancer is selected from ovarian cancer, cervical cancer, bladder cancer, esophageal cancer, and malignant melanoma, and prostate cancer.

133. **(provisionally-withdrawn, subject to rejoinder)** The method of Claim 128 where the cancer is non-small cell lung cancer.

134. **(provisionally-withdrawn, subject to rejoinder)** The method of Claim 128 where the cancer is glioblastoma.

135. **(provisionally-withdrawn, subject to rejoinder)** The method of Claim 130 where the gastrointestinal cancer is stomach cancer.

136. **(provisionally-withdrawn, subject to rejoinder)** The method of Claim 127 where the disease is selected from ischemic coronary artery disease, diabetic retinopathy, psoriasis and rheumatoid arthritis.

137. **(currently amended)** The compound of Claim 67 selected from

*N*-(3,4-dichlorophenyl)-6-(methyloxy)-7-{{[(8a*R*)-tetrahydro-1*H*-[1,3]thiazolo[4,3-*c*][1,4]oxazin-6-ylmethyl]oxy}quinazolin-4-amine;

*N*-(3,4-dichlorophenyl)-6-(methyloxy)-7-[(tetrahydro-1*H*-[1,3]thiazolo[4,3-*c*][1,4]oxazin-3-ylmethyl]oxy]quinazolin-4-amine; and

*N*-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-[(octahydro-2*H*-quinolizin-3-ylmethyl]oxy]quinazolin-4-amine; and

a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

138. **(currently amended)** The Compound of Claim 81 selected from

*N*-(4-bromo-2,3-dichlorophenyl)-7-{{[(3*R*,9*aS*)-hexahydro-1*H*-[1,4]oxazino[3,4-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;

*N*-(4,5-dichloro-2-fluorophenyl)-7-{{[(3*R*,9*aS*)-hexahydro-1*H*-[1,4]oxazino[3,4-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-5-chloro-2-fluorophenyl)-7-{{[(3*R*,9*aS*)-hexahydro-1*H*-[1,4]oxazino[3,4-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;

*N*-(3-chloro-2,4-difluorophenyl)-7-{{[(3*R*,9*aS*)-hexahydro-1*H*-[1,4]oxazino[3,4-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;

*N*-(3,4-dichloro-2-fluorophenyl)-7-{{[(3*S*,9*aS*)-hexahydro-1*H*-[1,4]oxazino[3,4-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-3-chloro-2-fluorophenyl)-7-{{[(3*S*,9*aS*)-hexahydro-1*H*-[1,4]oxazino[3,4-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;

<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-<{[(3 <i>S</i> ,9 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichlorophenyl)-7-<{[(hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-<{[(3 <i>S</i> ,9 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-<{[(3 <i>S</i> ,9 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-<{[(3 <i>S</i> ,9 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-<{[(3 <i>R</i> ,9 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine; <u>and</u>
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-<{[(3 <i>R</i> ,9 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -[1,4]oxazino[3,4- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine; <u>and</u>
a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

139. (currently amended) The Compound of Claim 81 selected from

<i>N</i> -(3,4-dichlorophenyl)-7-<{[(3 <i>R</i> ,8 <i>a</i> <i>R</i> )-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-<{[(3 <i>S</i> ,8 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichlorophenyl)-7-<{[(3 <i>S</i> ,8 <i>a</i> <i>R</i> )-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichlorophenyl)-7-<{[(3 <i>S</i> ,8 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichlorophenyl)-7-<{[(3 <i>R</i> ,8 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-<{[(3 <i>S</i> ,8 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-<{[(3 <i>S</i> ,8 <i>a</i> <i>S</i> )-hexahydro-1 <i>H</i> -pyrrolo[2,1- <i>c</i> ][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;

*N*-(3-chloro-2,4-difluorophenyl)-7-{{[(3*S*,8*aS*)-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-2,3-dichlorophenyl)-7-{{[(3*S*,8*aS*)-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine; and

*N*-(4,5-dichloro-2-fluorophenyl)-7-{{[(3*S*,8*aS*)-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine; and

a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

140. (currently amended) The Compound of Claim 84 selected from

*N*-(3,4-dichloro-2-fluorophenyl)-7-({[(3*aR*,6*aS*)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3*aR*,6*aS*)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

7-({[(3*aR*,6*aS*)-2-acetyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-*N*-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(3*aR*,6*aS*)-octahydrocyclopenta[c]pyrrol-5-ylmethyl]oxy} quinazolin-4-amine;

*N*-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3*aR*,6*aS*)-2-(methylsulfonyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine;

*N*-(3,4-dichloro-2-fluorophenyl)-7-({[(3*aR*,6*aS*)-2-ethyoctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3*aR*,6*aS*)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine;

*N*-(3,4-dichloro-2-fluorophenyl)-7-({[(3*aR*,6*aS*)-2-methyoctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3*aR*,6*aS*)-2-methyoctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(3-chloro-2,4-difluorophenyl)-7-({[(3*aR*,6*aS*)-2-methyoctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(4,5-dichloro-2-fluorophenyl)-7-({[(3*aR*,6*aS*)-2-methyoctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-5-chloro-2-fluorophenyl)-7-({[(3a*R*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-2,3-dichlorophenyl)-7-({[(3a*R*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(3,4-dichlorophenyl)-7-({[(3a*R*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a*R*,6a*S*)-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; and

*N*-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3a*R*,6a*S*)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine; and

a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

**141. (currently amended) The Compound of Claim 84 selected from**

*N*-(3-chloro-2,4-difluorophenyl)-7-({[(3a*R*,5*s*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(3-chloro-2,4-difluorophenyl)-7-({[(3a*R*,5*r*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-2,3-dichlorophenyl)-7-({[(3a*R*,5*s*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(4-bromo-2,3-dichlorophenyl)-7-({[(3a*R*,5*r*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

*N*-(3,4-dichlorophenyl)-7-({[(3a*R*,5*s*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; and

*N*-(3,4-dichlorophenyl)-7-({[(3a*R*,5*r*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; and

a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

142. (currently amended) The Compound of Claim 87 selected from

<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
7-({[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-2-acetoxyoctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)- <i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-octahydrocyclopenta[c]pyrrol-5-ylmethyl]oxy}quinazolin-4-amine;
ethyl (3 <i>aR</i> ,6 <i>aS</i> )-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydrocyclopenta[c]pyrrole-2(1 <i>H</i> )-carboxylate;
ethyl (3 <i>aR</i> ,5 <i>r</i> ,6 <i>aS</i> )-5-[(4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl)oxy]methyl]hexahydrocyclopenta[c]pyrrole-2(1 <i>H</i> )-carboxylate;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-2-(methylsulfonyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>s</i> ,6 <i>aS</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>s</i> ,6 <i>aS</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6 <i>aS</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>s</i> ,6 <i>aS</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

<p><i>N</i>-(4,5-dichloro-2-fluorophenyl)-7-({[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;</p>
<p><i>N</i>-(4-bromo-5-chloro-2-fluorophenyl)-7-({[(3a<i>R</i>,5<i>s</i>,6a<i>S</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;</p>
<p><i>N</i>-(4-bromo-5-chloro-2-fluorophenyl)-7-({[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;</p>
<p><i>N</i>-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;</p>
<p><i>N</i>-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine;</p>
<p>1,1-dimethylethyl (3a<i>R</i>,6a<i>S</i>)-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyl-oxy)quinazolin-7-yl]oxy}methyl)hexahydrocyclopenta[c]pyrrole-2(1<i>H</i>)-carboxylate;</p>
<p><i>N</i>-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy}quinazolin-4-amine; and</p>
<p>1,1-dimethylethyl (3a<i>R</i>,6a<i>S</i>)-5-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl) hexahydrocyclopenta-[c]pyrrole-2(1<i>H</i>)-carboxylate; and</p>
<p>a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.</p>

143. (currently amended) The Compound of Claim 84 selected from

<p><i>N</i>-(3,4-dichloro-2-fluorophenyl)-7-({[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;</p>
<p><i>N</i>-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;</p>
<p>7-{{[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-2-acetyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy}-<i>N</i>-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)quinazolin-4-amine;</p>
<p><i>N</i>-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy}quinazolin-4-amine;</p>
<p>ethyl (3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-5-[(4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl)oxy]methyl]hexahydrocyclopenta[c]pyrrole-2(1<i>H</i>)-carboxylate;</p>
<p><i>N</i>-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(3a<i>R</i>,5<i>r</i>,6a<i>S</i>)-2-(methylsulfonyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy}quinazolin-4-amine;</p>

<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>s</i> ,6a <i>S</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3-chloro-2,4-difluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4,5-dichloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-5-chloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-2,3-dichlorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(3,4-dichlorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;
<i>N</i> -(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine; and
1,1-dimethylethyl (3 <i>aR</i> ,6 <i>aS</i> )-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyl-oxy)quinazolin-7-yl]oxy}methyl)hexahydrocyclopenta[c]pyrrole-2(1 <i>H</i> )-carboxylate;
<i>N</i> -(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{{[(3a <i>R</i> ,5 <i>r</i> ,6a <i>S</i> )-octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy}quinazolin-4-amine; and
1,1-dimethylethyl (3 <i>aR</i> ,6 <i>aS</i> )-5-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl) hexahydrocyclopenta-[c]pyrrole-2(1 <i>H</i> )-carboxylate; and
a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

144. (previously presented) The Compound of Claim 143 selected from *N*-(3,4-dichloro-2-fluorophenyl)-7-({[(3a*R*,5*r*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; *N*-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3a*R*,5*r*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; and *N*-(3,4-dichloro-2-fluorophenyl)-7-({[(3a*R*,5*s*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; and optionally as a pharmaceutically acceptable salt thereof.

145. (previously presented) The pharmaceutical composition of Claim 144.

146. (currently amended) The Compound of Claim 143 selected from 1,1-dimethylethyl (3a*R*,6a*S*)-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydrocyclopenta[c]pyrrole-2(1*H*)-carboxylate; *N*-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{[(3a*R*,5*r*,6a*S*)-octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy}quinazolin-4-amine; *N*-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{[(3a*R*,5*r*,6a*S*)-octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy}quinazolin-4-amine; 1,1-dimethylethyl (3a*R*,6a*S*)-5-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl) hexahydrocyclopenta[c]pyrrole-2(1*H*)-carboxylate; and a single geometric isomer, stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

147. (previously presented) The Compound of Claim 144 named *N*-(3,4-dichloro-2-fluorophenyl)-7-({[(3a*R*,5*r*,6a*S*)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine optionally as a pharmaceutically acceptable salt thereof.

148. (previously presented) The pharmaceutical composition of Claim 147.

149. (currently amended) The Compound of Claim 96 selected from

(3*S*,9a*S*)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydro-2*H*-pyrido[1,2-a]pyrazin-1(6*H*)-one;

(3*S*,9a*R*)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydro-2*H*-pyrido[1,2-a]pyrazin-1(6*H*)-one;

(3*S*,8*aS*)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydropyrrolo[1,2-a]pyrazin-1(2*H*)-one;  
(3*S*,8*aR*)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydropyrrolo[1,2-a]pyrazin-1(2*H*)-one;  
(3*S*,8*aS*)-3-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydropyrrolo[1,2-a]pyrazin-1(2*H*)-one; and  
(3*S*,8*aS*)-3-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-2-methylhexahydropyrrolo[1,2-a]pyrazin-1(2*H*)-one; and  
a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

150. **(currently amended)** The Compound of Claim 99 selected from

*N*-(3,4-dichlorophenyl)-7-{{[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)methyl]oxy}-6-(methyloxy)quinazolin-4-amine;  
*N*-(3,4-dichlorophenyl)-7-{{[(3-*endo*)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]methyl}oxy}-6-(methyloxy)quinazolin-4-amine; and  
7-{{[(3-*endo*)-8-azabicyclo[3.2.1]oct-3-ylmethyl]oxy}-*N*-(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine; and  
a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

151. **(canceled)**

152. **(currently amended)** The Compound of Claim 120 selected from

1,4:3,6-dianhydro-5-({[4-[(4-bromo-5-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5-deoxy-2-*O*-methyl-D-xylo-hexitol;  
1,4:3,6-dianhydro-5-deoxy-5-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-2-*O*-methyl-D-glucitol;  
1,4:3,6-dianhydro-5-deoxy-5-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-2-*O*-methyl-D-xylo-hexitol;  
1,4:3,6-dianhydro-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5-deoxy-2-*O*-methyl-D-xylo-hexitol;  
1,4:3,6-dianhydro-5-({[4-[(3-chloro-2,4-difluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5-deoxy-2-*O*-methyl-D-xylo-hexitol;

1,4:3,6-dianhydro-5-( {[4-[(4-bromo-2,3-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5-deoxy-2- <i>O</i> -methyl-D-glucitol;
1,4:3,6-dianhydro-2-deoxy-2-( {[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-5- <i>O</i> -methyl-D-threo-hexitol; <u>and</u>
1,4:3,6-dianhydro-5-deoxy-5-( {[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)-2- <i>O</i> -methyl-D-glucitol; <u>and</u>
a single stereoisomer, racemate, enantiomer, or diastereomer, thereof and optionally as a pharmaceutically acceptable salt thereof.

Claims 153-154 (**canceled**)

155. **(currently amended)** A pharmaceutical composition comprising a compound of Formula I as defined in Claim 67 or 143~~any one of Claims 67, 79, 84, 89, 96, 99, 138, 139, 140, 141, 142, 143, 146, and 150~~ or Ia as defined in Claim 113~~any one of Claims 113, 114, and 152~~ and a pharmaceutically acceptable carrier.